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EXAMINER	
SIMS, JASON M	

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1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,270	FOX ET AL.	
	Examiner	Art Unit	
	JASON M. SIMS	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-10,19,21,23,24,28,29 and 39-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10,19,21,23,24,28,29 and 39-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/8/2009 has been entered.

Applicants have amended their claims, filed 9/8/2009, and therefore rejections newly made in the instant office action have been necessitated by amendment.

Applicant has newly added claim 47 in the response filed 9/8/2009, which has been acknowledged and entered.

Claims 4-10, 19, 21, 23, 24, 28-29, and 39-47 are the current claims hereby under examination.

Claim Rejections - 35 USC § 101

Response to Arguments

Applicant's arguments, filed 8/7//2009 and 9/8/2009, with respect to the rejection of claims under 35 USC 101 have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejection has been withdrawn.

Claim Rejections - 35 USC § 112 First Paragraph

Response to Arguments

Applicant's arguments, filed 8/7//2009 and 9/8/2009, with respect to the rejection of claims under 35 USC 112 First have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejection has been withdrawn.

The following rejection is being newly made upon further considerations:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 5 comprises a step wherein signature probes comprise a moiety selected from the group consisting of RNA, DNA, an analog of RNA or DNA including peptide nucleic acids, 2-O-methyl DNA and any other molecule that can interact with the test sample, wherein the wording "any other molecule that can interact with the test sample nucleic acid in a sequence-specific way" lacks support in the instant specification. Support for "any other molecule," such as ribosomal proteins, antibodies, or any regulatory element, etc. has not been found in the specification. As such, claim 5 lacks adequate written description of sufficient species to show possession of the genus of "any other molecule."

Claim 9 and all claims dependent thereon are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the method wherein the defined grouping comprises a moiety selected from the group consisting of: a specific genus, species, serotype, and another grouping below the species level, but does not reasonably provide enablement for the moiety of race. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to define a grouping on the tree of relationship based on race, and practice the invention commensurate in scope with these claims.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must make or perform the method of claim 4, specifically step D wherein one of the nodes includes race, i.e. a defined grouping on the tree of relationship comprises a moiety of race. For the reasons discussed below, undue experimentation would have been required to practice the claimed invention.

b) The specification provides guidance for making and using a defined grouping comprising a specific genus, species, or serotype, but does not provide guidance for defining a grouping based on race. In other words, the specification does not provide guidance as how to go about assigning probes or establishing genetic relationships within the tree based on "race."

c) The specification does not provide any working examples of how to establish or define genetic relationships within the tree based on race, such as what probes to assign.

e) State of the art is complicated and unpredictable.

f) The skill of those in the art of molecular biology is high.

g) The prior art is devoid of how to divide groups genetically within a phylogenetic tree based on race, thus one of ordinary skill in the art would not know how to establish such genetic relationships within the tree based on race. One of skill in the art would not know how to assign or create a database of signature probes or establish genetic relationships within the tree based on race.

The skilled practitioner would first turn to the instant specification for guidance to practice methods of how to establish genetic relationships within the tree based on race. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art is devoid of such teachings. Finally, said practitioner would turn to trial and error experimentation to determine how to create such a tree of relationship based on race. Such represents undue experimentation.

Claim Rejections - 35 USC § 112 Second Paragraph

Response to Arguments

Applicant's arguments, filed 8/7//2009 and 9/8/2009, with respect to the rejection of claims under 35 USC 112 Second have been fully considered and are persuasive because of applicant's amendments and arguments. Therefore the rejection has been withdrawn.

The following rejection is being newly made upon further considerations:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28-29 and all claims dependent therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 and all claims dependent therefrom comprises a step, which is unclear as to what information it provides from the "formula." In other words, the step comprises calculating a "signature quality function" using a formula, which comprises the presence of sequences in a particular group of organisms or viruses and their presences in other organisms NOT belonging to that group of organisms or viruses, i.e. the sequences appear to belong to any and all groups. Therefore, it is unclear as to what comprises the "single formula" and what information is derived from it when a sequence that belongs in anything and everything is included. Clarification via clearer claim wording is required.

Claim 29 and all claims dependent therefrom comprises two formulas for which values of "Qs" are calculated, wherein it is vague and indefinite as to which formula is used for the calculation. The step of claim 29 recites calculating the value of Qs by "the equation" and then recites two equations (one not apparently being the simplified version of the other) for which Qs can be calculated. Thus it is vague and indefinite as which equation is being used for said calculation. Clarification via clearer claim wording is required.

The following rejection is being newly applied, which has been necessitated by amendment:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4-9, 19, 21, 24, and 39-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al. (US P/N 6,797,817).

The claims are directed to a method for determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:

A) Obtaining or creating a nucleic acid sequence database of the same target nucleic acid, from all organisms or viruses that will be incorporated into the determination;

B) Obtaining or developing a bifurcating node phylogenetic tree having multiple nodes that establishes the genetic affinity between the organisms or viruses included in the nucleic acid sequence databases;

C) Optionally computationally fragmenting each target nucleic acid sequence such fragmentation being performed in a programmed computer so as to create a subsequence database of nucleic acid subsequences of length N that occur in at least two sequences in the nucleic acid database, where N is at least seven;

D) Tabulating in a programmed computer the extent to which the presence of each particular nucleic acid sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationship by examining the occurrence frequency of each subsequence in the target nucleic acid of the organisms and viruses encompassed by or not encompassed by each node in the tree; to create a database of characteristic signature sequences;

E) Deriving a plurality of signature probes from a signature-database of characteristic signature sequences that will be complementary to a portion of the target nucleic acid sequence of the organism or virus if the signature sequence is present;

F) Hybridizing the signature probes to the target nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the target nucleic acid of the organism or virus and detecting such signals;

G) Identifying the nodes in the bifurcating node phylogenetic tree of genetic relationship that are represented by the signature probes that produced detectable

signal, in order to determine the genetic affinity of the organism or virus in the test sample.

With regards to limitations of claims 4, 40, 43, and 45: Ebersole et al. teach at Col. 9, lines 35-45 that a phylogenetic Tree of Life was obtained and used for extracting sequences that represented the major microorganism domains, Bacteria and Archeae, which could be used as signature sequences for obtaining signature probes for testing for the presence of dechlorinating bacteria. Ebersole et al. further teach at the abstract, Figs. 1 – 2, and col. 5, lines 27-34, that the 16s rRNA regions, i.e. the target nucleic acid, are analyzed from the samples and organisms wherein their profiles/sequence database have been created, which reads on steps A) – B). Step C) is an optional step, not necessarily performed in the instant method. However, Ebersole et al. at col. 5, lines 40-45 and col. 9, lines 11-19 and line 46 teach identifying consensus sequences, which are subsequences which occur most frequently in the 16S target nucleic acid of the organisms from which a 16s DNA profile was created. Ebersole et al. further teach at col. 9, lines 54-56 examples of the consensus sequences wherein the sequences are of length 7 or more (see SEQ ID NO: 34), which reads on limitations of step C). Ebersole et al. further teach at col. 4, lines 55-67 and col. 5, lines 1-4, lines 40-45, col. 8, lines 1-19, col. 9, lines 11-19 and lines 54-56 using sequence analysis software in a computer to analyze the consensus sequence, wherein the consensus sequences were found in each decholorinating organism, and that the use of particular sequences, i.e. signature regions/sequences, may be used to identify decholorinators as well as for genetic sub-typing of species. Furthermore, Ebersole et al. teach at col.

9, lines 46-54 that signature regions of subsequence length N (7 or more) were analyzed and found to be characteristic of different organisms, which reads on limitations of step D) and claim 45. Ebersole et al. teach at col. 4, lines 55-67 and col. 5, lines 1-4, that sequence profiles, from which signature probes are derived, may be used to identify and subtype bacteria with similar metabolic pathways. Therefore, a signature probe may be used to identify a dechlorinated bacteria and/or bacteria with similar metabolic pathways, such as subspecies of decholorinates, which further reads on steps E) - G). Ebersole et al. at col. 5, lines 34-39, col. 6, lines 31-34, col. 6, lines 58-67, and col. 7, lines 1-9 teach using signature sequences for generating probes and defines the use of probes and hybridization as such that is consistent in the art, which produce detectable signals, which further reads on step E). Ebersole et al. further teach at col. 2, lines 51-65, the use of signature probes in hybridizing to identify sequences such that a signal is detectable, which further reads on step F). Ebersole et al. teach at col. 8, lines 38-40 that the sequences are useful for the identification of new dechlorinating bacteria, as well as for sub-typing strains of Dehalococcoides ethenogenes. Furthermore, Ebersole et al. teach at col. 9, lines 19-40 that sequences used for obtaining probes and closest or nearest organisms to these sequences were determined, which further reads on step G).

Ebersole et al. suggest, but do not explicitly teach tabulating the extent to which the presence of each particular subsequence of length N is characteristic of each node in the bifurcating phylogenetic tree of genetic relationship by examining the occurrence

frequency of each subsequence in the target nucleic acid to create a database of characteristic signature sequences.

Ebersole et al. suggest this because they teach at col. 5, lines 40-45 and col. 9, lines 11-19 and lines 46-56 using software to analyze the consensus sequence, which are a set of bases which occur most often in the 16S sequences of the organisms and are characteristic of the group of decholorinating organisms. Ebersole et al. further teach determining signature regions and sequences for identifying particular organisms, which are characteristic of those organisms.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have tabulated the extent to which the presence of each particular subsequence of length N is characteristic of each node in the bifurcating phylogenetic tree of genetic relationship by examining the occurrence frequency of each subsequence in the target nucleic acid to create a database of characteristic signature sequences in the method taught by Ebersole et al. This is because Ebersole et al. already considers how particular sequences are characteristic of individual and groups of organisms. One of skill in the art would have recognized that applying the known technique of tabulating the extent to which the sequences were characteristic of each node (i.e. group or individual organism) would have yield predictable results.

Ebersole et al. teach claims 5 and 41 -42 at col. 2, lines 50-59 wherein rDNA are used for obtaining probes, which reads on the use of DNA for comprising signature probes.

Ebersole et al. teach claim 6 at col. 6, lines 58-67 wherein hybridization is taught which is consistent in the art wherein a hybridization step is done in solution, which reads on claim 6.

Ebersole et al. teach claim 7 at col. 13, lines 25-30 wherein it is taught that probes which generate a detectable signal are used, which makes obvious a probe wherein the detection step utilizes radioactive labels, chemiluminescence, and/or fluorescence.

Ebersole et al. teach claim 9, of defining a grouping of a specific species, i.e. dechlorinating bacteria, see Col. 9, lines 35-45.

Ebersole et al. teach limitations of claim 10 as follows: at col. 9, lines 45-67 and col. 10 Ebersole et al. teach using a 16S rDNA profile of the isolated dechlorinators to compile profiles, i.e. database, of at least 12 nucleic acid sequenes (col.10, lines 40-49 describe at least 12 different variations of sequences usable for diagnostics of the dechlorinating bacteria) as in step A). Ebersole et al. further describes variations of subsequences and at Fig. 1-2 and table 2 tabulates these differences and distributions as in step B). Ebersole et al. further evaluates the extent to which subsequence variation is characteristic of each species of dechlorinating bacteria, i.e. node, which reads on step C).

Ebersole et al. suggest, but do not explicitly teach wherein the tree comprises 11 or more nodes as in claim 39 and a limitation in claim 45.

Ebersole et al. suggest this because they teach at col. 1-2 a method of identifying several species of dechlorinating bacteria, which uses phylogenetic relationships.

Ebersole et al. further teach at col. 2, lines 60-65 being able to identify new strains of dechlorinating bacteria.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used a tree comprising 11 or more nodes for use in the method of identifying bacteria as taught by Ebersole et al. This is because Ebersole et al. teach a method of using a tree of nodes for help in identifying dechlorinating bacteria. It would have been obvious to one of ordinary skill in the art that as new/ i.e. more dechlorinating bacteria are identified, see col. 2, lines 60-65, that any phylogenetic tree used in the identification process would also comprise more nodes. Therefore, the use of 11 or more nodes in a phylogenetic tree opposed to fewer than 11 nodes, is a result of an optimized parameter and not the product of innovation. The differences between the claimed invention and the prior art were encompassed in known variation or in a principal known in the prior art.

Ebersole et al. suggest, but do not explicitly teach where the same target nucleic acid sequence is obtained from at least 12 organisms or viruses as in claim 44 and a limitation of claim 45.

Ebersole et al. suggest this because they teach at col. 1-2 a method of identifying several species of dechlorinating bacteria, which uses phylogenetic relationships and several nucleic acid sequences. Ebersole et al. further teach at col. 2, lines 60-65 being able to identify new strains of dechlorinating bacteria.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used the same target nucleic acid sequence obtained from at

least 12 organisms or viruses for use in the method of identifying bacteria as taught by Ebersole et al. This is because Ebersole et al. teach a method of using a tree of nodes for help in identifying dechlorinating bacteria. It would have been obvious to one of ordinary skill in the art that as new/ i.e. more dechlorinating bacteria are identified, see col. 2, lines 60-65, that more sequences would be used in the identification process. Therefore, the use of sequences from 12 or more organisms or viruses fewer organisms or viruses, is a result of an optimized parameter and not the product of innovation. The differences between the claimed invention and the prior art were encompassed in known variation or in a principal known in the prior art.

Ebersole et al at col. 9 and col. 10, teach using consensus sequences for identifying signature regions, i.e. signature sequences, wherein the sequences comprise at least 12 (see the 16s rDNA base substitutions of the consensus sequences, which when taken independently or together are usable for a diagnostic for dechlorinating bacteria), and the consensus sequences are at least 30% identical over at least one subsequence of at least 50 nucleotides (see SEQ ID NO: 34) as in claim 46.

Ebersole et al. teach at col. 9, lines 46-65 teach using consensus sequences of length 7 or longer that occur in all the dechlorinating isolates when creating a profile, i.e. database of signature sequences as in claim 47.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al. (US P/N 6,797,817) as applied to claim 4 above, and further in view of Coleman et al. (US P/N 6,738,502).

Ebersole et al. teach claim 4 as described above in the instant office action.

Ebersole et al. suggest do not explicitly teach generating the bifurcating phylogenetic tree of relationship by parsimony method.

Ebersole et al. suggest this because they teach using and creating a phylogenetic tree of organisms and in particular bacteria.

Coleman et al. teach at col. 2, lines 45-49 and col. 5, lines 50-57 a method directed to using 16S rRNA sequence information to deduce a phylogenetic relationship based on a parsimony method.

It would have been obvious to one ordinary skill in the art at the time of the instant invention to have used a parsimony method for creating a phylogenetic relationship as taught by Colman et al. for use in the method of using sequences and phylogenetic relationships for identifying bacteria as taught by Ebersole et al. Creating a phylogenetic tree by a parsimony method is a well known method as taught by Coleman et al. One of ordinary skill in the art would have substituted one known element, i.e. deducing a phylogenetic tree based on parsimony for another method of deducing a phylogenetic tree, and the results of the substitution would have been predictable. The differences between the claimed invention and the prior art were encompassed in known variations or in a principal known in the prior art.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/ Jason Sims /

/Marjorie Moran/

Supervisory Patent Examiner, Art Unit 1631